Progress and puzzles

A wealth of data is now available on the functional organization of the human visual cortex. Caution is necessary in basing interpretations of such data on information gained from studies of the monkey visual cortex.

Recent anatomical and, especially, brain-imaging studies have provided new and exciting data on the functional organization of the human visual cortex ([1–7], for example). In particular, there have been reports of cortical architecture, brain regions activated by particular modes of stimuli and instruction, and activation patterns associated with tasks designed to reveal retinotopic organization (that is, an organization in which neighboring cortical neurons represent neighboring retinal positions). These studies clearly provide new and important insights into the functional organization of visual cortex in humans, but some of the results remain open to several interpretations.

Present notions about the organization of the human visual cortex are, of course, strongly influenced by current theories of visual cortex organization in monkeys. These theories have, in turn, been influenced by Brodmann's early conclusion that the visual cortex in humans and other primates includes an area (17 or V1) that is nearly surrounded by two concentric rings, designated areas 18 and 19. Early experimental evidence on cortical connection patterns in monkeys was thus interpreted within the framework of an area V1, also known as the striate cortex, bordered successively by ring-like areas V2 and V3. There are now reasons to question the validity of V3 in monkeys, and thus its existence in humans. But V3 is just one of over 30 visual areas that have been proposed for monkeys. Thus, the broader issue here concerns the validity of current proposals for visual cortex organization in monkeys, and their use in guiding experimental studies and data interpretation in humans.

V1, V2 and MT (V5) seem well established

Visual area V1 is such a distinctive subdivision of the cortex that it can be identified by almost any method. Thus, from its histological appearance alone, both early and subsequent investigators have agreed on the location of V1 in humans (Fig. 1a) and other primates. This is certainly not the case for any other visual area, and hence there was no agreement among Brodmann and his contemporaries on how the extrastriate cortex is organized [8]. Modern investigators have access to much more information than histological appearance, and we have the potential for greater certainty and consensus. Most importantly, the recognition that data produced by any single experimental approach typically contain ambiguities has led to the view that, to be reliable, the definition of a visual area should be based on congruent results obtained using several different procedures. Thus V2, which presents the clear advantage of having an unquestionable border with V1, has been defined by electrophysiologically revealed retinotopy, retinotopic patterns of connections with V1, and architectonic and other distinctions. The fortunate discovery in monkeys that V2 can be unequivocally delineated by the modular banding pattern in cytochrome-oxidase- and myelin-stained preparations, especially in sections cut parallel to the surface, led to a way of precisely delineating V2 in humans ([5,6], for example). The recent imaging studies of Sereno *et al.*, [1] provide new identifying information on the retinotopy of V2 in humans.

The middle-temporal visual area (MT or V5) can also be identified with a high degree of certainty in the human brain. While MT is best defined by a concordance of data on retinotopic organization, input patterns from V1 and V2, and architectonic features, the field is so distinctly dark in myelin and cytochrome-oxidase stained preparations that it can be reliably outlined in these preparations alone, especially when brain sections have been cut parallel to the surface. MT has thus been identified architectonically in humans [5,6]. MT is also unusual in that it contains a population of neurons that are highly activated by moving stimuli and are insensitive to parameters of color. This distinctive feature has allowed MT to be reliably visualized in positron emission tomography (PET) and magnetic resonance imaging (MRI) studies ([3,4], for example).

Evidence for other visual areas is more equivocal

Evidence for other visual areas has typically been more limited and much less compelling. For example, V3, conceived as a visual area that lies along the full length of V2 and mirrors V2 in retinotopic organization, was first defined by the input pattern from only limited portions of V1. Supporting evidence for the existence of V3 in monkeys, such as compatible retinotopic patterns of activation, has accumulated (see [2]), but seemingly incompatible findings have emerged as well. Most notably, the dorsal and ventral halves of V3 have such differences in their connections, architectonic appearance and neuronal response properties that many investigators have considered them to be two separate visual areas, dorsal V3 (V3d) and the ventroposterior area (VP). Sereno *et al.* [1] favor this V3d-plus-VP interpretation of their retinotopic mapping data for human visual cortex (Fig. 1b), even though the results seem equally consistent with the existence of a single V3 area.

An unsettling feature of the notion of V3d as a separate visual area is that it would be an area that represents only

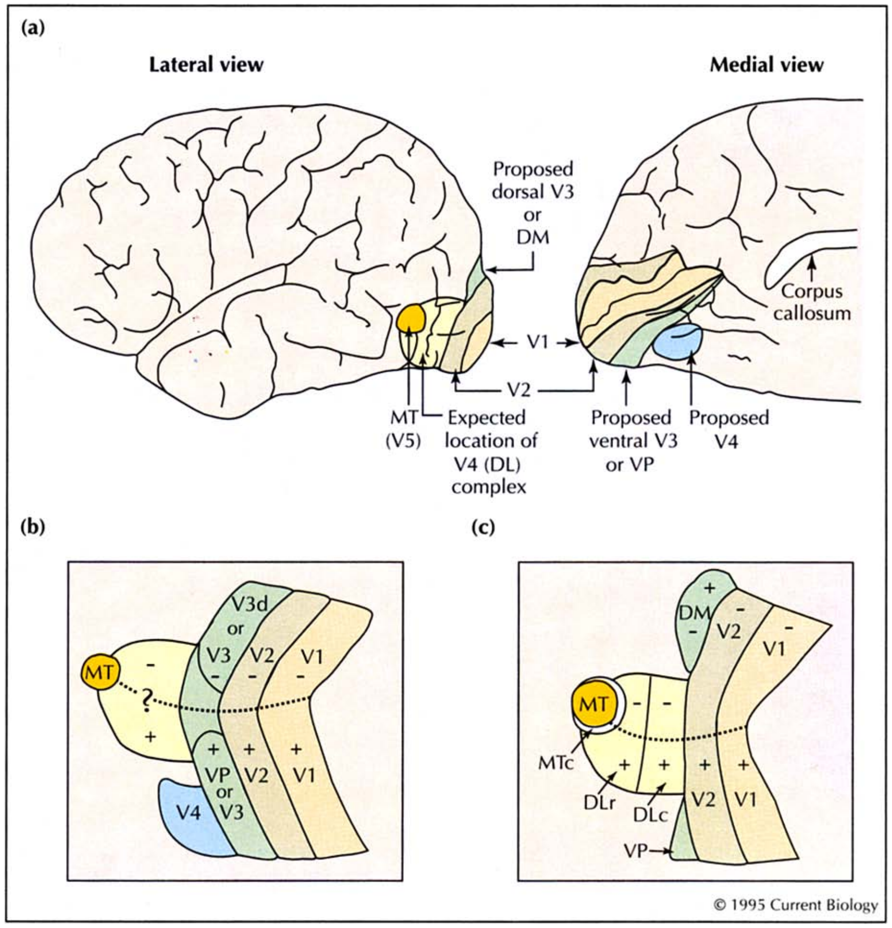

Fig. 1. Theories of visual cortex organization. Three visual areas, V1, V2 and MT (V5) have been well defined in monkeys and now in humans. Other subdivisions are less certain, and several possibilities are illustrated here. **(a)** Lateral and medial views of a human brain, showing the locations of V1, V2 and MT, and the proposed and expected (from comparative studies on other primates) locations of the V4 or DL complex. Note the locations of proposed dorsal V3 (or DM) and ventral V3 (or VP). **(b)** Arrangement of human visual areas V3d, VP and V4 suggested by Sereno *et al.* [1]. The alternative view [2] is that V3d and VP join to form a single visual area, V3. V4 was originally defined in macaque monkeys as a region between V2 and MT — the corresponding human region is indicated by a question mark. The dashed black line from V1 to MT divides visual areas into halves representing the upper (+) or lower (–) visual quadrants. **(c)** Our proposal for the arrangement of visual areas in monkeys [9–11]. Instead of a dorsal V3 representing only the lower visual quadrant, we have a larger dorsolateral visual area, DM, representing both upper and lower quadrants. Between MT and V2, we divide the former V4 region into a crescent-shaped area around MT (MTc) and rostral and caudal dorsolateral areas (DLr and DLc). Representations of the upper (+) and lower (–) visual quadrants are marked.

the lower visual quadrant, a seemingly improbable feature. Based on early studies of New World monkeys, we have argued that existing data on macaques are more compatible with the view that much of V3d and some adjoining tissue belong to a dorsomedial visual area, DM (Fig. 1c), which represents both the upper and lower quadrants and has connections with both dorsal and ventral parts of V1 and V2 (see [9]). The point here is not to argue for our interpretation, but to stress that at least three interpretations are compatible with most available data. Thus, it seems premature to apply dogmatically any specific theory based on monkeys to humans.

Similar uncertainties exist about the organization and extent of the V4 region (see [10] for review). V4 was originally identified in macaque monkeys by inputs from V2 and V3. Its location between V2 and MT, estimated extent and retinotopic organization were so similar to the electrophysiologically mapped dorsolateral visual area, DL, of New World owl monkeys (see [10]) that there seemed little reason to doubt that different terms were being applied to the equivalent visual area. Subsequently, on the basis of electrophysiological mapping evidence, V4 has been portrayed as extending far into the ventral temporal lobe (see [1]), although none of the original territory was given up. Supporting evidence for this extension in terms of the input from V2 is lacking. Furthermore, additional evidence on connections, architecture and retinotopic patterns in New World monkeys has led us [10,11] to reinterpret DL as a region containing three distinct fields, MTc, DLr and DLc (Fig. 1c). In macaque monkeys, more limited evidence also suggests that the original V4 region contains three visual areas [12]. Thus, we might expect the V4 region of humans to be a composite of several visual areas.

In humans, a ventromedial territory, associated with the processing of color information, has been proposed as the homologue of V4 (Fig. 1a; see [7] for review). Sereno *et al.* [1] have recently postulated a similar location for V4 (Fig. 1b). One difficulty with this proposal is that it places V4 in a position far removed from the location originally proposed for V4 in monkeys. The relative position of structures has long been regarded as an important clue to homology, and the unexpected location of the proposed V4 in humans would seem to require some explanation. A related issue is why the original V4 region of monkeys and the proposed V4 region of humans seem to be involved in different aspects of visual processing (see [7]).

How do we reason from monkeys to humans?

Phylogenetic groups are distinguished by morphological and behavioral differences, and the degree of difference between taxa is assumed to increase with phylogenetic distance. Old World monkeys represent the closest phylogenetic group to humans that is accessible for intensive study, and thus studies on macaques should have the most potential for guiding interpretations of the human brain. Nevertheless, humans are not macaques, nor did we evolve from macaques. How can we legitimately use information from macaques to understand cortical organization in humans?

The basic premise of taxonomic classification is that members of the group share features not found in other groups. Thus, the presence of a corpus callosum distinguishes eutherian from other mammals, and it is highly unlikely that any unstudied eutherian mammal would fail to have this feature. This logic can be applied to the visual system. We expect to find V1 and V2 in humans precisely because they seem to be present in all or nearly all mammals. Because clear evidence for MT has been obtained in all primates examined, although not in other mammals, we would be astonished if MT were absent in humans.

For visual areas where the only evidence comes from macaques, we should be far less certain, as such areas could be specializations of macaques. In this regard, it is puzzling that some investigators seem to have no conceptual difficulty in assuming that the organization of the visual cortex is basically the same in macaques and humans, while accepting as valid major differences in the proposed organization of visual cortex in New and Old World monkeys. If New and Old World monkeys can diverge so much in visual cortex organization, why not monkeys and humans? After all, we have been evolving separately for over 20 million years.

References

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